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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/802,110 | 03/07/2001 | James Leushner | VGEN.P-058-2 | 5580 |

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|---|---|
| WILDER, CYNTHIA B | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/802,110 | LEUSHNER ET AL. | |
| | Examiner | Art Unit | |
| | Cynthia B. Wilder, Ph.D. | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *14-25 and 27-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-25 and 27-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/2/2006 has been entered.

***Status of the claims***

Claims 14 has been amended. Claims 1-13 and 26 have been canceled. Claims 14-25 and 27-36 are pending.

### *Claim Objections*

*2.* Claim 17 is objected to because of the following informalities: The claim 17 is objected to because it depends from a canceled claim 13. For the purpose of application of prior art, the claims 17 will be examined as depending from the claim 14. Appropriate correction is required.

### *Claim Rejections - 35 USC § 102*

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 14-17, 20-22, 25, 27-29, 32-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Digby et al (US 6,432,634 B1, filing date April 18, 1996). Regarding claims 14-

16, 21, 25, 27-28, 33, Digby et al teach a kit for sequencing a specific region from a gene, said kit consisting of, in package combination at least one reaction vessel or a plurality of reaction vessels for each of the regions to be sequenced containing a mixture of a plurality of sequencing primers, one for each gene region to be evaluated. The plurality of sequencing primers each comprising a reactive portion which specifically hybridizes with the DNA in the sample and a label portion, the label portions of the primers being different and distinguishable one from the other (col. 7, lines 11-20). Digby et al further teach wherein kit may further comprise a thermally stable polymerase enzyme, deoxynucleotide triphosphate feedstock, dideoxnucleotide triphosphate and buffer (col. 3, lines 1-9 and col. 6, lines 58-60). Digby et al teach that the kit and method are useful for evaluating a desired target sequence in a plurality of sample (col. 1, lines 47-54). The binding of the primers to the sense and antisense strands of the DNA in a desired sample is an inherent property of the primers.

Regarding claim 17, 22, 29 and 34, Digby et al teach the kit of claim 14, wherein the kit includes four deoxynucleotide triphosphate and at least one dideoxynucleotide triphosphate (col. 3, lines 1-9).

Regarding claims 20 and 32, Digby et al teach wherein the kit includes as a non-specific reagent a polymerase enzyme, THERMOSEQUENASE (col. 6, lines 5-7), which is the same polymerase enzyme that Applicant uses in the instant kit. Therefore, the limitation extending nucleic acid polymer at a rate which is no less than 0.4 times the rate of incorporation of deoxynucleotides is an inherent property of the polymerase enzyme, THERMOSEQUENASE.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 18-19, 23, 24, 30, 31, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Digby et al (US 6,432,634) and Ruano (5,427,911, patent date June 27, 1995) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14, (1994). Regarding claims 18, 19, 23, 24, 30, 31, 35 and 36, Digby et al teach a kit for sequencing a desire gene in a sample, said kit consisting of, in package combination at least one reaction vessel or a plurality of reaction vessels for each of the regions to be sequenced containing a mixture of a plurality of sequencing primers, one for each gene region to be evaluated. The plurality of sequencing primers each comprising a reactive portion which specifically hybridizes with the DNA in the sample and a label portion, the label portions of the primers being different and distinguishable

one from the other. Digby et al further teach wherein kit may further comprise a thermally stable polymerase enzyme, deoxynucleotide triphosphate feedstock, dideoxnucleotide triphosphate and buffer.

Digby et al do not expressly teach wherein the dideoxynucleotide triphosphate is present in a mole ratio to the corresponding deoxynucleotide triphosphate of from 1:50 to 1:1000 or 1:100 to 1:500.

Ruano et al. teach a method for sequencing genomic DNA sample, the method comprising amplifying in vitro with two locus specific primers that flank both ends of the target region to obtain a template, synthesizing simultaneously truncated strands from both ends of the template by introducing a dideoxynucleotide terminator for each of the four bases adenine, guanine, cytosine and thymine and introducing a label or labels specific for either or both of the 5' ends of the synthesizing strands, thermally cycling steps to provide a sufficiently readable signal (col. 2, lines 3-23). Ruano further teaches wherein the dideoxynucleotide triphosphate is in a mole ratio of about 1:10 to the corresponding deoxynucleotide triphosphate (col. 6, lines 47-68).

The reference of Ruano differs from the instant invention in that the reference does not teach wherein the method comprises the dideoxynucleotide triphosphate in a mole ratio of 1:50 to 1: 1000 or in a mole ratio of 1:1000 to 1:500 to the corresponding deoxynucleotide triphosphates.

In a method similar to that of Ruano, Rao teaches a method of direct sequencing of polymerase chain reaction-amplified DNA. Rao teaches wherein the method comprises mixing the PCR-amplified genomic DNA, labeled primer sequencing buffer and Taq polymerase in a

tube, adding to the mixture in four separate tubes, four dNTPs and at least one dideoxynucleotide triphosphate, perform thermal cycling (see Table 3, page 5). Rao differs from the instant invention in that Rao does not teach wherein the mole ratio of the ddNTP:dNTP is from 1:50 to 1:1000 or 1:100 to 1:500. Rao also does not teach wherein the polymerase enzyme incorporates dNTPs into an extending nucleic acid polymerase at a rate which is no less than 0.5 times the rate of incorporation of dNTPs. However, Rao discloses that the composition of the dNTP/ddNTP mix varies depending on the type of polymerase preparation used. Rao states that different polymerases require different dNTP/ddNTP ratios for optimal chain terminations and therefore, the reagents or kits for one polymerase cannot be substituted with those for a different polymerase. Rao further teaches that optimal buffer conditions for the synthesizing reaction will vary based on the specific DNA polymerase used (see Table 3 legend). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claim invention that the mole ratio of ddNTP to dNTP in the kit of Digby would vary depending on the specific polymerase utilized as taught by Rao. Further, both Digby and Rao teach wherein the polymerase used is THERMOSEQUENASE, which is the same enzyme as used by Applicant.

***Applicant's Traversal***

7. Applicant traverses the rejection on the following grounds: Applicant summarizes the instant invention and summarizes the Examiner's rejections. Applicant states that the rejection improperly ignores claim limitations that require the kits to contain sequencing primers for both the sense and antisense strands of the target region of interest and therefore fails to compare the prior art with all limitations of the claims. Applicant states that the Examiner has rejected the claims based on a claim construction that effectively limits the claim to a "kit comprising a single reaction vessel containing a mixture of region, specific sequencing reagents, wherein said

region specific reagents comprise region specific primers", which claim construction completely ignores the claim language:

> "consisting of, in package combination", "for each DNA region to be sequenced", "sufficient for sequencing the sense and antisense strand of each DNA region to be sequenced and optionally in said mixture one or more non-region specific sequencing reagents", " and said optional non-region specific sequencing reagents are selected from one or more of the group consisting of deoxynucleotide triphosphate feedstock, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer".

Applicant asserts that the above construction of the claim which ignores the limitations recited above is in error. Applicant stats that the phrase "region specific sequencing reagents sufficient for sequencing the sense and antisense strands of each DNA region to be sequenced" constitutes a limitation that inherently requires structural elements or region specific primers for both the sense and antisense strands. Applicant contends that without primers for both the sense and antisense strands, the recited function of "sequencing the sense and antisense strands of each DNA region" could not be accomplished. Applicant asserts that the functional language of claim 14 does not in fact require the necessary structural limitations. Applicant states that he teaching of the cited prior art cannot meet the limitation that is "sufficient for sequencing the sense and antisense strands of each DNA region to be sequenced". Applicant concludes that the claims are patentably distinct over the cited prior art.

***Examiner's Response***

8. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In regards to Applicant's arguments concerning improper claim construction, it is noted that the claim limitations: "consisting of, in package combination", "for each DNA region to be sequenced", "sufficient for sequencing the sense and antisense strand of each DNA region to be sequenced and optionally in said mixture one or more

non-region specific sequencing reagents" are considered an "intended use of the components of the kit. The non-region specific reagents in the claims are "optional" features of the kit that are not critical to the novelty of the kit. MPEP states "a recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. MPEP further states that "language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation" (see MPEP 2111.02).

In regards to Applicant's arguments that the phrase "region specific sequencing reagents sufficient for sequencing the sense and antisense strands of each DNA region to be sequenced" constitutes a limitation that inherently requires structural elements or region specific primers for both the sense and antisense strands, it noted that the claims are drawn to a product, not a method. The limitations phrase "sufficient for sequencing the sense and antisense strands of each DNA region to be sequenced" and "wherein .... a pair of primers which specifically bind to the sense and antisense strands and flank one of the DNA regions" are not specific sequences outside of the kit that do not impart functionality to the components of the lit. Limitations as recited above provides no sequence of the primers or specific DNA sequence as the target. No functionally (sequence) is given as to what the primers bind to. Furthermore, how the primers bind (e.g., specifically to the sense and antisense strand of a DNA region to be sequences) relates to a use and not a component of the kit. Thus, the properties of the primers in the kit are not clear.

To reiterate, the claims are drawn to a kit, not a method. The kit itself, cannot perform any function, but rather only provides reagents that can function in a method for sequencing. Such limitations as "specifically binding to the sense and antisense strands" in relations to the primers, do not provide any structurally features or properties of the primers, bur rather only suggest an intended use of the primers when employed in a sequencing method. Again MPEP states that a recitation of an intended use of the claimed invention must result in *a structural difference* between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In order to provide structural properties of the lit, specific sequences of the primers or target, such as identified by "SEQ Id NO:" would be required and this impart functionality to the kit because it would clearly identify how and/or to what the primers bind for use in sequencing. The Examiner maintains that the claim construction is proper.

***Conclusion***

9. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637

7/9/2006